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F. Aaron Dubberley
(Print Name)

F. Aaron Dubberley
(Signature)

Date: July 9, 2001

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application

Matzinger et al.

Group: 1624

Serial No. 09/546,143, filed April 10, 2000

Examiner: Truong, T.

For: **ASYMMETRIC SYNTHESIS PROCESS**

RESPONSE UNDER 37 CRF 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1624

RESPONSE

Nutley, New Jersey 07110
July 9, 2001

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Applicants respond to the final Office Action dated April 9, 2001 by traversing all rejections of the claims and respectfully requesting a Notice of Allowance for this application.

The allowance of claims 10, 11 and 27 and the Examiner's statement that the subject matter of claims 13, 16, 18, 20, 22 and 24 are allowable are appreciatively acknowledged.

Cited Prior Art Fails to Anticipate Instantly Claimed cis-Configuration

The rejection of claim 23 under 35 U.S.C. 102(a) over either Lampe et al. or Adams et al. is improper and should be withdrawn. Applicants respectfully refer the Examiner to Formula X of claim 23, which clearly shows the hydroxyl and amino groups to be in a cis formation to each other (both groups are on the same side of the ring structure). The compounds cited by the Examiner as anticipating claim 23 (compound 25 of Lampe et al. and compound 20 of Adams et al.) both clearly show a trans formation for the hydroxyl and amnio groups, meaning that each group is on a different side of the ring structure. The trans-configuration taught by Lampe et al. and Adams et al. does not encompass the cis compounds of claim 23.

The rejection of claim 25 under 35 U.S.C. 102(a) over Adams et al. is improper and should be withdrawn. Again, the instant claim specifies a cis arrangement between the hydroxyl group and the NHR^1 group, whereas the compound cited by the Examiner, compound 21 of Adams et al., has a trans arrangement. The trans-configuration taught by Adams et al. does not encompass the cis compounds of claim 25.

The rejection of claim 25 under 35 U.S.C. 102(a) over the disclosure of compounds B1-23 of Barbier et al. is improper and should be withdrawn. The exemplified compounds of Barbier et al. are all in the trans formation (3R, 4R). Again, the teaching of the trans formation does not anticipate the instantly claimed, structurally distinct, cis formation.

The rejection of claim 17 under 35 U.S.C. 102(a) over the disclosure of compounds 12 and/or 13 of Krogsgaard-Larsen et al. is improper and should be withdrawn. Compound 13 of Krogsgaard-Larsen et al. has a trans configuration between the hydroxyl and ester groups. Since compound 13 of Krogsgaard-Larsen et al. does not encompass the compounds of claim 17, which have a cis configuration between the hydroxyl and ester groups, compound 13 fails to anticipate claim 17.

Compound 12 of Krogsgaard-Larsen et al. is a racemic mixture of trans-hydroxy esters, including *both* a compound according to instant formula (VIII) *and* the other possible trans-hydroxy ester enantiomer, which is depicted as compound 12 in Scheme 2 of Krogsgaard-Larsen et al. However, claim 17 excludes the racemic mixture disclosed as compound 12 in Krogsgaard-Larsen et al., because claim 17 has a limitation requiring the absence of substantial amounts of enantiomers of the claimed compounds. Furthermore, since Krogsgaard-Larsen et al. fails to teach or suggest any motivation or method for separating the racemic mixture into substantially pure isomers, Krogsgaard-Larsen et al. fails to enable or make obvious the instantly claimed enatiomerically pure compounds of formula (VIII).

Barbier et al. Fails to Place the Compounds of Claims 25 and 26 in Public Domain

The rejection of claims 25 and 26 under 35 U.S.C. 103 over Barbier et al. is improper and should be withdrawn. Barbier et al. fails to place the compounds of instant claim 25 in the public domain because 1) the generic chemical formula III of Barbier et al. fails to disclose the instantly claimed compounds and/or 2) Barbier fails to provide an enabling disclosure of the instantly claimed compounds.

As the Examiner has correctly pointed out, a "generic chemical formula will anticipate a claimed species covered by the formula when the species can be 'at once envisioned' from the formula." Here, the instantly species of claim 25 cannot be "at once envisioned" from the generic chemical formula III of Barbier et al. Applicants respectfully submit that formula III of Barbier et al. encompasses millions of compounds. Note that A in the formula, is defined as in column 1, lines 20-30, can encompass any of at least 6 different ring structures with each and every ring atom being optionally substituted by lower-alkyl, lower-alkoxy and hydroxy groups, with some ring atoms having additional possible substitutents. Therefore, each position of each ring structure has at least 12 possible substituents, or $12^5 \cong 250{,}000$ possibilities per ring structure. Once

all six possible ring structures are considered, there are at least 1.5 million possibilities. And once particular enantiomers of each of those compounds are taken into consideration, the number will be even greater. Applicants respectfully submit that the Examiner has yet to present any reason why the instantly claimed specific enantiomers can be "at once envisioned" from such a large group of possibilities. Accordingly, this rejection is improper and must fail.

The rejection of claims 25 and 26 under 35 U.S.C. 103 over Barbier et al. is also improper because Barbier fails to provide an enabling disclosure for the instantly claimed compounds (see MPEP 2121.02). The compounds of claims 25 and 26 are specific cis stereoisomers. These specific stereoisomers are necessary to obtain the object of the invention, the asymmetric synthesis of a biologically useful class of stereoisomers. Barbier et al. fails to teach or suggest to one of skill in the art how to make any cis isomers. Applicants respectfully note that *all* of the examples taught by Barbier (B1-23) are trans isomers. The disclosure of Barbier et al. leaves one of skill in the art with no direction as to how to make the cis compounds of claims 25 and 26. Accordingly, this rejection is improper and must fail.

"Amino-Protecting Group" is Not Indefinite and is Enabled Under §112

Reconsideration and withdrawal of the rejection of claims 12, 14, 15, 17, 19, 21, 23 and 25 under 35 U.S.C. 112, first and second paragraph, as being indefinite or requiring undue experimentation to practice, are respectfully requested. This rejection has been made over the term "amino-protecting group", which is alleged in the final Office Action to be both indefinite and non-enabled.

The term "amino-protecting group", as used in the rejected claims, is well-known in the art to which this invention belongs, organic synthesis. The claimed "amino-protecting group" is a well known class of materials, all of whose members would be recognizable to one skilled in the art. As a demonstration of this, we searched the issued

patent claims of the past 25 years on the USPTO website and found 588 patents with the term "amino protecting group" in the claims. Applicants have also previously submitted a copy of the table of contents for Chapter 7, "Protection for the Amino Group" from Protective Groups in Organic Synthesis by Theodora W. Green, published in 1981 by John Wiley & Sons, Inc. As shown in the table of contents for that particular chapter, "amino protecting groups" are well-known and exemplified by many members, all of which are within the skill of the art of organic synthesis. As shown by such wide-spread and text-book use, this term is well-known in the art.

Terms that define a well-known class of materials, the members of which would be ascertainable to one skilled in the art, comply with 35 U.S.C. 112, first and second paragraph. In this manner, terms such as "water soluble hydrolyzable carbohydrate", *In re Skoll*, 187 USPQ 481 (CCPA 1975); "organic and inorganic acids", *In re Skoll*, supra; "inorganic salts", *In re Fuetterer*, 138 USPQ 217 (CCPA 1963); "polymerizable materials", *In re Bowen*, 181 USPQ 48 (CCPA 1974); and "organic radical", *In re Robins*, 166 USPQ 552 (CCPA 1970) have been held to comply with 35 U.S.C. 112, first and second paragraph.

The fact that the instant term "amino-protecting group" covers many different substituents is not a sufficient basis for a rejection under 35 U.S.C. 112. As stated by the CCPA in holding that the term "organic and inorganic acids" is not indefinite under 35 USC 112:

> We first consider the expression 'organic and inorganic acids', which is said to be indefinite and of uncertain scope. We cannot agree. Although there are undoubtably a large number of acids which come within the scope of 'organic and inorganic acids', the expression is not for that reason indefinite. We see no reason to believe that the public would be confused as to what subject matter is circumscribed by applicant's claim. *In re Skoll*, supra at 482.

The "amino-protecting group" term improperly rejected in this application is no less rigorously defined than the "organic and inorganic acids" upheld by the CCPA in *Skoll*. As noted above, applicants' "amino-protecting group" defines a

well known class of substituents used in chemical synthesis, all of whose members would be recognizable to one skilled in the art.

The definition of the R^4 groups of the claims by their particular function, being amino-protecting groups, and not by particular chemical structures also fails to make the term or the claims indefinite under 35 U.S.C. 112. In reversing a 35 U.S.C. 112 rejection of a claim term to "an inorganic salt that is capable of holding a mixture of said carbohydrate and protein in colloidal suspension in water", the CCPA specifically approved use of such functional limitations:

> It is true that appellant's inorganic salt *is* defined in terms of "what it does" rather than "what it is." We note, however, that the Supreme Court, in a seldom quoted passage in the Wabash case, stated, 37 USPQ at 469:
>
> > A limited use of terms of effect or result, which accurately define the essential qualities of a product to one skilled in the art, may in some instances be permissible and even desirable ...
>
> Appellant in the instant case has made just such a use of terms of result to define an essential quality of his inorganic salts. (Emphasis in original) *In re Fuetterer*, supra at 222.

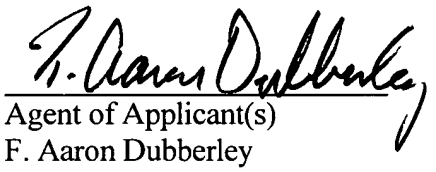
Accordingly, the instant rejection of claims under 35 U.S.C. 112 for containing the term "amino-protecting group" is improper and should be withdrawn. "Amino-protecting group" defines a well-known and understood class of chemical groups, all of whose members would be recognizable to one skilled in the art; the instant term, claiming groups with the functional limitation that they are amino protecting, accurately defines the essential qualities of those particular groups to one of skill in the art; and the simple fact that the term is broad does not make it indefinite.

Regarding the allegation that "amino-protecting group" is non-enabled in the instant claims because only one species is disclosed in the specification, Applicants again refer to the text-book chapter cited above. This text-book chapter is just one example of a whole host of knowledge about the identity and use of amino-protecting groups that

was known to the skilled organic chemist at the time that this application was filed. It is not necessary for an Applicant to teach in the specification what is well-known in the art, and amino-protecting groups are well-known in the art. Therefore, the applicant is not required to provide the specification with *any* examples of amino-protecting groups, much less the exhaustive listing required by implication in the final Office Action.

Applicants respectfully request that a timely Notice of Allowance be issued for this application.

Respectfully submitted,



Agent of Applicant(s)
F. Aaron Dubberley
(Reg. No. 41001)
340 Kingsland Street
Nutley, New Jersey 07110
Telephone: (973) 235-4387

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Telefax: (973) 235-2363